REMARKS

Applicants respectfully request reconsideration of the application in view of the foregoing amendments and the following remarks.

Claims 42-56 are currently pending upon entry of the amendments. Claims 1-41 have been canceled, without prejudice. Claims 51-55 have been canceled as they were withdrawn by the Examiner. Claims 42, 44 and 47-48 have been amended.

Allowable Subject Matter

Claim 56 was stated to be allowable.

The Examiner indicated that Claims 42-43 would be allowable if the claims were rewritten in independent form including all the limitations of the base claims and any intervening claim(s). Applicant has rewritten Claim 42 as advised. An indication of the allowability of Claims 42 and 43 is respectably requested.

Rejections under 35 U.S.C. 112, 2nd paragraph

Claims 44-50 were rejected as indefinite.

Claims 44 and 48 were cited as unclear in how cultivating determines productivity. Applicant has amended the claims to correct a grammatical error by replacing [[by]] with after. The clonal subtypes are tested after growth in the fermentation flasks.

Claim 47 was cited as being unclear in how isolating colonies will purify them. Applicant has amended Claim 47 to more clearly describe the subject matter by pointing out that the colonies are picked and re-plated to purify them. Applicant refers to the Specification at page 13, line 33 – page 14, line 11 as an example.

Rejections under 35 U.S.C. 112, 2nd paragraph

Claims 1, 40 and 41 were rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Cress et al., in view of Korz et al., in further view of Voziyanov et al. Applicants respectfully traverse. However, in efforts to speed prosecution, these claims have been canceled, without prejudice to presenting the recited subject matter in a further application.

Claim 3 was rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Cress et al., Korz et al. and Voziyanov et al. in further view of Mason et al. Applicants respectfully traverse. However, in efforts to speed prosecution, the claim has been canceled, without prejudice to presenting the recited subject matter in a further application.

Claim 9 was rejected under 35 U.S.C. § 103 as being allegedly unpatentable over Cress et al., Korz et al., Voziyanov et al. and Mason et al., in further view of Kongo et al. Applicants

respectfully traverse. However, in efforts to speed prosecution, the claim has been canceled, without prejudice to presenting the recited subject matter in a further application.

Request for Teleconference

If the Examiner believes that the prosecution of this application could be advanced by a teleconference, the Examiner is invited to contact Applicant's attorney at the number below. The Examiner is also invited to contact the undersigned attorney if clarification is required on any aspect of this response, or if any of the claims are considered to require further amendment to be placed in condition for allowance after entry of this Amendment.

Conditional Petition

Applicant herein makes a conditional petition for any relief available to correct any defect found in connection with this paper or the application.

In view of the amendments and comments herein, Applicants respectfully take the position that all claims are in proper form for allowance and earnestly solicit a favorable action on the merits.

Respectfully submitted,

By /Michael D. Yablonsky Reg. # 40,407/
Michael D. Yablonsky, Ph.D.
Reg. No. 40,407
Attorney for Applicant

MERCK & CO., INC.
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Rahway, New Jersey 07065-0907
(732) 594-1932

Date: 27 April 2010

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Chartrain, M. *et al.*		
Serial No.:	10/588,295	Case No.: 21502P	Art Unit: 1636
Filed:	August 4, 2006		Examiner: Joike, Michele
For:	PROCESS FOR LARGE SCALE PRODUCTION OF PLASMID DNA BY *E. COLI* FERMENTATION		Conf. No.: 8419

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT UNDER 35 U.S.C. § 1.111

Dear Sir:

In response to the Office Action mailed 28 January 2010, please enter the following amendments and consider the foregoing remarks. No petition for additional time is believed to be necessary. However, Applicant conditionally petitions for any time found to be necessary. Please charge any fee due to Deposit Account No. 13-2755. Please credit any overpayment or charge any fee deficiency to Deposit Account No. 13-2755.

AMENDMENTS TO THE CLAIMS are reflected in the listing of claims which begins on page 2 of this paper.

REMARKS begin on page 6 of this paper.

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims

Claims 1-41. (Canceled)

Claim 42. (Currently Amended) A process for production of plasmid DNA comprising:

(a) selecting a highly productive clonal subtype of a strain of *E. coli* transformed with a DNA plasmid comprising:

(i) observing a phenotypic heterogeneity in a population of colonies generated by the transformed *E. coli*, and selecting as potentially highly productive clonal subtypes those colonies that represent a minor component of said phenotypic heterogeneity in said population of colonies;

(ii) purifying said potentially highly productive clonal subtypes and determining the productivity of said purified, potentially highly productive clonal subtypes by measuring the plasmid copy number per cell; and,

(iii) selecting as a highly productive clonal subtype a potentially highly productive clonal subtype that exhibits a higher plasmid copy number per cell in comparison to non-selected, transformed *E. coli* clonal subtypes of the same strain; and,

(b) cultivating said highly productive clonal subtype with fed-batch fermentation in chemically-defined medium in a fermentation volume of greater than about 1000L,

wherein said phenotypic heterogeneity is observed after the transformed *E. coli* is grown on blood agar at about 30°C, and

~~The process of claim 41,~~ wherein the potentially highly productive clonal subtypes that represent the minor component of said phenotypic heterogeneity are gray colored-colonies while the major component of said phenotypic heterogeneity are white-colored colonies.

Claim 43. (Previously Presented) The process of claim 42, wherein the potentially highly productive clonal subtypes are purified from the blood agar.

Claim 44. (Currently Amended) The process of claim 43, wherein the plasmid copy number per cell of the purified, potentially highly productive clonal subtypes is determined [[by]]

after cultivating said clonal subtypes in a shake flask with feeding fermentation system using chemically defined medium.

Claim 45. (Previously Presented) The process of claim 44, wherein said strain of *E. coli* is DH5.

Claim 46. (Previously Presented) The process of claim 45, wherein said chemically-defined medium comprises a medium selected from the group consisting of Medium C, Medium D, Medium E, Medium F and Medium G.

Claim 47. (Currently Amended) The process of claim 41, wherein the potentially highly productive clonal subtypes are purified by picking bacteria from ~~isolating~~ colonies from a second type of agar that does not contain blood products, wherein said picked colonies correspond to the gray-colored colonies formed on the blood agar, and plating the bacteria picked from said colonies on said second type of agar.

Claim 48. (Currently Amended) The process of claim 47, wherein the plasmid copy number per cell of the purified, potentially highly productive clonal subtypes is determined [[by]] after cultivating said clonal subtypes in a shake flask with feeding fermentation system using chemically defined medium.

Claim 49. (Previously Presented) The process of claim 48, wherein said strain of *E. coli* is DH5.

Claim 50. (Previously Presented) The process of claim 49, wherein said chemically-defined medium comprises a medium selected from the group consisting of Medium C, Medium D, Medium E, Medium F and Medium G.

Claim 51 - 55. (Canceled)

Claim 56. (Previously Presented) A process for production of plasmid DNA comprising:

(a) selecting a highly productive clonal subtype of a strain of *E. coli* transformed with a DNA plasmid comprising:

(i) observing a phenotypic heterogeneity in a population of colonies generated by the transformed *E. coli* when incubated on blood agar at 30°C consisting of a minor

component of gray-colored colonies and a major component of white-colored colonies, and selecting as potentially highly productive clonal subtypes the gray-colored colonies;

(ii) purifying said potentially highly productive clonal subtypes, and determining the productivity of said purified, potentially highly productive clonal subtypes by measuring the plasmid copy number per cell; and,

(iii) selecting as a highly productive clonal subtype a potentially highly productive clonal subtype that exhibits a higher plasmid copy number per cell in comparison to non-selected, transformed *E. coli* clonal subtypes of the same strain; and,

(b) cultivating said highly productive clonal subtype with fed-batch fermentation in chemically-defined medium.

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Date: 27 April 2010